Arguments/Remarks

Claims 1, 15-17, 19-20, 22, and 24 - 26 have been cancelled. Claims 2-14, 18, 21, and 23 are currently pending. Claims 2-5, 18, and 21 have been amended. Reconsideration of the amended claim set is respectfully requested.

Rejections Under 35 U.S.C. 112

Claims 1-2, 15, 18-21, and 23-26 have been rejected under 35 U.S.C. § 112, first paragraph as not being enabled. More particularly, the Examiner alleges that the specification does not enable the compounds of formula (I) wherein two vicinal R1 substituents together with the carbon atoms of the phenyl ring (to which the two R1 substituents are attached) for a heterocyclic ring.

The claims have been amended to exclude this embodiment. The rejection is therefore moot. Withdrawal and reconsideration are respectfully requested.

The Examiner has also rejected claims 15, 18-21, 24, and 26 under 35 U.S.C. § 112, first paragraph as not being enabled. Claims 15, 19-20, 24, and 26 have been cancelled.

Claims 18 and 21 are still pending. It is unclear what the Examiner finds non-enabled in the claims however. To the extent the Examiner finds the "method of preventing" objectional, the phrase has been deleted by the cancellation of claim 19.

Claim 21 claims a method of treating a disease which responds to "inhibition of IGF-1R in a mammal." The Examiner states in the Office Action at the bottom of page 5 to the top of page 6:

> The specification at pages 33-35 provides in vitro assays to measure the IGF-1R tyrosine kinase inhibition activity. Based on the inhibition activity, the specification provides that the compounds are useful as inhibitors of IGF-1R tyrosine kinase, and therefore useful in the treatment of a variety of diseases, including all types of cancer. The instant claims appear to be 'reach through' claims.

The present claims however, as the Examiner points out are limited to inhibition of IGF-1R. They are further restricted to compounds of formula (I). The compounds have been enabled as inhibitors of IGF-1R, and there is not attempt to reach through to other small molecule inhibitors of IGF-1R. Withdrawal and reconsideration are respectfully requested.

Claims 2, 4, 7-15, 18, and 25 have been rejected under 35 USC §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the

subject matter which applicant regards as the invention. Applicants have amended the claims to delete each of the objectionable subject matter. Withdrawal and reconsideration are respectfully requested.

Rejection Under 35 USC §101

Claim 15 has been canceled, and the rejection is therefore moot. Withdrawal and reconsideration are requested.

Rejections Under 35 USC §102

Claims 15, 18-20, 25, and 26 have been rejected under 35 USC §102 as being anticipated by WO04/005282 to Furet. Each of these claims has been canceled. Withdrawal and reconsideration are requested.

Rejections Under 35 USC §103

Claims 1-15, 18-21, and 23-26 are rejected under 35 USC §103 as being obvious over Furet et al (WO04/005282) (Furet '282).

Claims 1, 15, and 20 have been canceled. Independent claims 1 and 21 now represent the broadest scope of the claimed invention. As currently standing, claims 1 and 21 represent a number of differences with Furet '282. The biggest distinction is that the variable Z in the present claim set is fixed as benzyloxy which is attached to the phenyl group in the meta position.

The Examiner has not established a prima facia case of obviousness. The Federal Circuit recently addressed obviousness of closely-related chemical structures in *Takeda Chem. Indus., Ltd. v. Alphapharm Pty., Ltd.*, 492. F.3d 1350 (Fed. Cir. 2007). Specifically citing their decision of *In re Deuel*, 51 F3d 1552, the Court stated, "A known compound may suggest its homolog, analog, or isomer because such compounds 'often have similar properties and therefore chemists of ordinary skill would ordinarily contemplate making them to try to obtain compounds with improved properties'." The Court clarified however, "that in order to find a prima facie case of unpatentability in such instances, a showing that the 'prior art would have suggested making the specific molecular modifications necessary to achieve the claimed invention' was also required."

The Court further held in *Takeda*, "Thus in cases involving new chemical compounds, it remains necessary to identify some reason that would have led a chemist to modify a known compound in a particular manner to establish a prima facie obviousness of a new claimed compound."

Still further, the CAFC has further elucidated the obviousness factors for chemical cases in *Eisai v. Dr. Reddy's Laboratories* (533 F.3d 1353) (Fed. Cir 2008). The CAFC discussed the *Graham* factors in new chemical composition cases that, "Post-KSR, a prima facia case of obviousness for a chemical compound still, in general, begins with the reasoned identification of a lead compound."

In this case, the Examiner has not put forth any reason why the compounds cited (example 23 from Furet reference) would be considered a lead compound from which an obviousness analysis should begin. It is improper to pick a random compound, such as compound example number 23 from Furet to begin the obviousness analysis.

Still further, there remains a need to identify a reason why modification of the prior art would occur to get the presently claimed structures. The Examiner therefore needs to identify a reason why example no. 23 would be considered a lead compound from which an obviousness analysis, and further identify a reason why modification thereof would be obvious. In the absence of such an analysis, a *prima facia* case of obviousness has not been established. Withdrawal and reconsideration are respectfully requested.

Double Patenting Rejection

Upon indication of allowable subject matter, applicant will address the double patenting rejection.

Should the Examiner have any questions, please contact the undersigned attorney.

Respectfully submitted,

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